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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/681,744	10/08/2003	Alex Turner	LEX-0460-USA	7298

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 04/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	**Application No.** 10/681,744	**Applicant(s)** TURNER ET AL.
	Examiner Q. Janice Li, M.D.	**Art Unit** 1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 21-24 are pending and under current examination.

Specification

The disclosure is objected to because it contains an embedded hyperlink (Specification, page 14) and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

The specification contains sequence disclosures (e.g. page 19, line 13) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2) but are not present in the Sequence Listing and/or identified in the specification by sequence identifier numbers. Applicant must provide sequence identifiers, in the case that these sequences are not included in the original sequence submission, a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). A full response to this Office Action must include a complete response to the requirement for a Sequence Listing.

Claim Rejections - 35 USC § 101 & 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 24 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The term “a host cell”, as recited in claim 24 encompasses the situation where the host cell is present or intended to be present in a human being (e.g. Specification, pages 23 and 27, § 5.4), then said cell becoming integrated into a human being and therefore being an inseparable part of the human itself. The scope of the claims, therefore, encompasses a human being, which is non-statutory subject matter. As such, the recitation of the limitation “isolated” and/or “non-human” would be remedial. See 1077 O.G. 24, April 21, 1987.

Claims 21-24 are rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility.

When determining whether an applicant has described the utility of invention, one has to determine whether the claimed invention has a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter.

A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying out further research to identify or reasonably confirm a real world" context use are not substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 6, Number 5, Pages 1092-1099).

The specification teaches that the present invention relates to the discovery, identification and characterization of novel polynucleotides (e.g. SEQ ID Nos: 1 or 3) that encode novel proteins (SEQ ID Nos: 2 or 4), which have unique primary sequence and share substantial sequence homology with a class of leucine rich repeat domain (LLRa)-containing proteins known to play an important role in signal transduction pathways. An example of such protein is the Ras suppressor protein-1 (RSU-1). The specification names the novel polynucleotides collectively as *SGT4*. The specification goes on to teach that *SGT4* is detected in various human tissues and at particularly high levels in skeletal muscle and heart. The specification teaches that the nucleic acid could be used for identifying cells expressing SGT4, for making antibodies, for research and nutritional use, and for screening assays such as compounds that modulate SGT4. However, the specification fails to disclose the actual sequence homology or the function of the *SGT4*, without such knowledge, one would not know how to use the polynucleotide, the encoded protein, and an antibody that recognizes SGT4 protein for a real world utility. For example, the specification fails to teach what percentage of homology is considered “substantial” to the sequence of RUS-1? Whether SGT4 has a similar or different function compared to Rus-1? Lacking the knowledge of *SGT4* function, one would not be know which criteria to use for a screening assay. Lacking the knowledge of what disease or condition is caused by *SGT4,* one would not know how to use it for nutritional purpose. Since the function of SGT4 is unknown, the antibody could only be used for research and development, which is not considered as a specific and substantial utility. Applicant is referred to the Revised Utility Examination Guidelines published December 21, 1999 in the Federal Register, Volume 64, Number 244, pages 71441-71442 for the required *specific* and *substantial* utility. "A CLAIMED INVENTION MUST HAVE A SPECIFIC AND SUBSTANTIAL UTILITY. THIS REQUIREMENT EXCLUDES 'THROW-AWAY' 'UNSUBSTANTIAL', OR 'NONSPECIFIC' UTILITIES," (column 3, 3rd paragraph of page 71441). According to the guidelines, utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not *substantial* utilities. A claim to a polynucleotide whose use is disclosed simply as "making antibodies or nutritional" would not be considered to be *specific* in the absence of a disclosure of a specific or a clearly depicted condition that may benefit from application of the polypeptide or antibody. Similarly, a general statement of a utility for further gene discovery, such as probing an unspecified gene, making a transgenic animal would ordinarily be insufficient in the absence of a disclosure of what particular gene or its disease association.

In the instant specification (pages 27-59), the disclosed utilities for the claimed polynucleotides are "identifying cells that express *SGT4*"; "making and using antibodies", "research uses"; "screening for compounds that bind to or modulate activity of *SGT4*", "nutritional uses", "making engineered cells or transgenic animals", or 'therapeutic uses", etc. However, since the function of *SGT4* is unknown, one would not know what to do with a compound that binds to *SGT4,* or what disease to treat. As such the disclosed vectors and host cells are only useful for the production of more polynucleotide or of polypeptides encoded thereby, and for further research, these asserted utilities apply to many unrelated human polynucleotide fragments and do not considered as specific and substantial utility in those instances where the final product, (polynucleotide for encoding a polypeptide, polypeptides, antibodies, antisense strands) has no disclosed or well-established utility.

With regard to the asserted utility for use as markers for tissues in which the corresponding protein is preferentially expressed either constitutively or at a particular stage of tissue differentiation or development or in disease states, the specification discloses that the *SGT4* can be detected in many different tissues, thus even though it may be highly expressed in skeletal muscle, it is not unique to the skeletal muscle. The specification fails to disclose whether other cells or tissues would also express such molecule, whether such expression is constitutive or stage-specific in the development and diseases. Since most genes are expressed in multiple tissues and cell types and some genes are expressed in all cell types, particularly if it is a protein in signal transduction pathway, the mRNAs corresponding to the claimed polynucleotide will most likely be also expressed in cells other than those disclosed in the specification. In the absence of information regarding all possible potential expression sites of the mRNA, one cannot use the claimed polynucleotide as a marker. The specification does not teach any use for a tissue marker, nor has any evidence of a well-established utility for such a use been provided.

With regard to the asserted utility of a nutritional supplement, the specification fails to disclose which disease or symptom is associated with SGT4 deficiency, nor has any evidence that such supplement would correct a nutritional deficiency been provided.

In view of the instant specification, the only readily apparent *immediate* utility for the disclosed polynucleotide is characterization of the polynucleotide itself in terms of map location, possibility of association with a disease gene, sequence of corresponding mRNA, cDNA, gene and polypeptide, identity of the function for the corresponding polypeptide and variants, *etc.* The sole *immediate* utility constitutes research on the claimed product itself (which is a non-statutory utility) in order to determine a specific and substantial statutory utility for the claimed invention. Practice of these disclosed utilities would first require further research on the disclosed sequences itself, i.e. there is no apparent immediate benefit to the public. *Brenner v. Manson*, 148 USPQ 689, 696 (US SupCt., 1966), noted that "CONGRESS INTENDED THAT NO PATENT BE GRANTED ON A CHEMICAL COMPOUND WHOSE SOLE 'UTILITY' CONSISTS OF ITS POTENTIAL ROLE AS AN OBJECT OF USE-TESTING", and stated, in context of the utility requirement, that "A PATENT IS NOT A HUNTING LICENSE. IT IS NOT A REWARD FOR THE SEARCH, BUT COMPENSATION FOR ITS SUCCESSFUL CONCLUSION."

Because the claimed invention is not supported by a specific and substantially asserted utility or a well-established utility for the reasons set forth above, credibility of the asserted utility cannot be assessed.

Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a well established utility for reasons set forth in the rejection under § 101 above, one skilled in the art clearly would not know how to use the claimed invention.

As noted above, the specification only provides guidance for the use of the recited polynucleotide for further experimentation in the elaboration of potential proteins encoded by the claimed polynucleotides that are functional in a signal transudation pathway; or for the use of the claimed nucleic acids in, for example, screening assay, tissue-type identification, or treating and diagnosing a disease. The first use represents an invitation to experiment wherein the artisan is invited to elaborate a functional use for the disclosed nucleic acids. The second use is premature at the time of filing since the functional characteristics of SGT4 and its association with any physiological condition was not known. Therefore, given the lack of guidance and direction in regard to what the polynucleotides would do and how one would use such, the artisan would be required to exercise undue experimentation in practice of the invention.

In view of the state of the art of protein technology with particular emphasis on using sequence homology for determining the function of the protein, *Everett et al* (Nat Genetics 1997;17:411-22) use sophisticated computational modeling based on sequence homology to determine that the gene product causing Pendred syndrome was a sulphate transporter. However, subsequent research and investigation into the actual functional properties of the protein revealed that the protein was actually a chloride-iodide transporter and not a sulphate transporter as was originally predicted based on sequence homology (*Scott et al,* Nat Genetics 1999 Apr;21:440-443). *Bork* (Genome Res 2000:10;398-400) teaches the power and pitfalls associated with comparative sequence analysis for predicting protein function, and points out that based on the observation that interacting proteins in one organism sometimes have homologs in other organisms, *Marotte et al* predicted novel interactions for 50% of yeast proteins using gene fusion information. However, they noted an overlap with classical methods and an error rate of 82% (left column in page 400). Therefore, according to the levels of the skill at the time of instant filing, determination of the function of a novel protein from sequence homology is not predictable. Therefore, the general knowledge and levels of skill in the art do not supplement the omitted disclosure, because specific, not general guidance is what is needed. As such, one skilled in the art would not know from an unspecified sequence homology, whether it is proper to place SGT4 in Rus-1 family, and what exactly SGT4 does in this family. Accordingly, because the specification fails to teach a specific function of the recited sequences, sequence homology alone is insufficient to provide an enabling disclosure for SGT4.

Further evidence that sequence homology cannot be used to predictably determine the function of a protein can be found in signal transduction protein family. For example, Rap is one of the Ras-like GTPase signal transduction proteins localized mainly at endocytic and lysosomal vesicles, and has an effector domain virtually identical to that of Ras, however, the function of Ras and Rap1 differ considerably in several aspects, Rap1 is considered to function as an antagonist of Ras signaling by trapping Ras effectors in an inactive complex (*Bos*, EMBO J 1998;17:6776-82, e.g.

abstract). Interestingly, a single threonine residue change at position 61 contributes to such differences; substitution of threonine for glutamine in Ras resulted in a strongly reduced intrinsic and GAP-induced GTPase activity (right column, page 6778). In view of such, from an unspecified sequence homology and incomplete disclosure of tissue distribution, one skilled in the art could not predictably associate SGT4 with the Rus-1 family or what it does in any signal transduction pathway. Therefore, the specification fails to provide an enabling disclosure for the asserted utility of the claimed invention.

As to the LRR-containing protein family, *Kobe et al* (Curr Opin Structure Biol 1995;5:409-16, IDS) teach, "THE KNOWN LRR-CONTAINING PROTEINS HAVE ONLY TWO THINGS IN COMMON: REPETITIVE SEQUENCES AND INVOLVEMENT IN PROTEIN-PROTEIN INTERATIONS". They teach the function of LRR proteins are extremely diverse, ranging from signal transduction, cell adhesion, development, DNA repair, recombination, transcription and RNA processing (e.g. page 410 and table 1). *Kobe et al* also teach often times, new repeats and structure indicates new functions (page 411). As such, it is highly unpredictable the functions of the SGT4 proteins assuming they indeed belong to the LRR protein family.

Therefore, in view of the limited guidance, the lack of predictability of the art and the breadth of the claims, one skill in the art could not practice the invention without undue experimentation as it is broadly claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites the limitation "a nucleic acid sequence of claim 24". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 21-24 are rejected under 35 U.S.C. 102(b) as being anticipated by *Suzuki et al* (Gene 1997;200:149-56).

Suzuki et al disclose an isolated nucleic acid molecule comprising the nucleotide sequence as described in instant SEQ ID No: 3, recombinant vector comprising the nucleic acid molecule, and host cells (human neuroblastoma cell line SK-N-MC) comprising the vector (e.g. page 150). Accordingly, *Suzuki et al* anticipate instant claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Dave T. Nguyen** can be reached on 571-272-0731. The **fax** numbers for the organization where this application or proceeding is assigned are **571-273-8300**.

Any inquiry of formal matters can be directed to the patent analyst, **Victor Barlow**, whose telephone number is (571) 272-0506.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Q. JANICE LI, M.D.
PRIMARY EXAMINER

Q. Janice Li, M.D.
Primary Examiner
Art Unit 1633

QJL
April 27, 2006